

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of: Eric Finzi

Application No. 10/773,785

Filed: February 6, 2004

Confirmation No. 7913

For: METHOD FOR TREATING DEPRESSION

Examiner: Vanessa L. Ford

Art Unit: 2856

Attorney Reference No. 6863-67727-01

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DECLARATION OF DR. ERIC FINZI UNDER 37 C.F.R. 1.132

1. I, Eric Finzi, M.D. Ph.D., am an inventor of the above-referenced application.

2. It is my understanding that claims 1-15 and 23-24 are rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Jahanshahi et al (Journal of Neurology, Neurosurgery and Psychiatry, 1992, 55:229-231) in view of Binder (U.S. Patent No. 5,714,468 published February 3, 1998) and further in view of Carruthers et al (U.S. Patent No. 6,358,917 B1 published March 19, 2002). Claims 16-21 were rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Jahanshahi et al., in view of Binder and Carruthers et al., further in view of Wagstaff et al. Torticollis is a positional abnormality of the head resulting from spasmodic neck muscles. Jahanshashi et al. teach the injection of Botulinium toxin into the superficial neck muscles (not facial muscles) of subjects to treat torticollis (see page 229, second column). Jahanshahi et al. report that the injection of botulinum toxin into the superficial neck muscles results in relaxation of the neck muscles, and straightening of the head and relief from neck pain, and *reduction of depression and disability associated with head position and pain* (page 231, first column). Jahanshahi et al. teach that depression in subjects with torticollis is “a reaction to the disorder” and that the improvement of depression was a “non-specific result” (page 231, second column). Jahanshahi et al. specifically do not study those subjects in which the torticollis was unaltered or worse following injection of Botulinium toxin into the neck muscles (see page 231, first column). Thus, Jahanshahi et al. do not describe the selection of specific subjects who have

depression as assessed by clinical criteria, nor do they disclose an effect of injection of Botulinum toxin into any other muscle except the neck.

Binder teaches the reduction of headache pain by injecting botulinum toxin. Binder et al. suggest the *extra-muscular* injection of botulinum toxin, at any site in the face, cranium or neck associated with pain (see the abstract). Binder et al. do not suggest, nor render obvious, the selection and treatment of any subject with dysthymia or major depression using clinical characteristics, nor does Binder et al. disclose administering a therapeutically effective amount of a neurotoxin directly into a muscle, let alone a corrugator supercilii or the procerus muscle to cause paralysis of the corrugator supercilii or the procerus muscle.

Caruthers et al. teach the cosmetic use of botulinum toxin to paralyze the depressor anguli oris muscle to alleviate downturn of a subject's mouth. Caruthers et al. do not disclose the administration of Botulinum toxin to the corrugator supercilii or the procerus muscle to cause paralysis of the corrugator supercilii or the procerus muscle.

There is nothing in any of the cited prior art that suggests selecting a subject with depression using the accepted clinical characteristics for these diseases, such as would be delineated in the Diagnostic and Statistical Manual of Mental Disorders, 4th edition (DSM-IV) or the Beck Depression Inventory, and then treating them with Botulinum toxin by injection into the corrugator supercilii or the procerus muscle. Furthermore, physicians, including psychiatrists, dermatologists (such as myself) and cosmetic surgeons, would not combine teachings on the treatment of torticollis with a treatment for a headache or with teachings of how to cosmetically improve the face.

3. Moreover, the injection of Botulinum toxin into the corrugator supercilii or the procerus muscle results in an unexpectedly superior result with regard to the treatment of depression, as compared to injection of the Botulinum toxin into the anguli oris muscle. This could not be predicted from the teachings of Jahanshahi et al., Binder, Carruthers et al., and/or Wagstaff et al., in any combination.

Results are presented in the specification for three patients. These patients were diagnosed with major depression or intermittent anxiety/depression. Botulinum toxin was administered to the corrugator supercilii or the procerus muscle of each of these subjects **using the presently claimed methods (see claims 1, 4-7, 8, 12-15 and 23-24). These studies were**

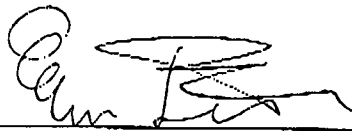


performed in the United States of America (US). The injections treated the depression of all of these subjects, who all reported improvements in their mood.

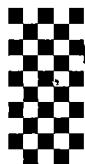
4. Injection of Botulinum toxin into other muscles of the face, such as the lateral obicularis oculi and the frontalis muscle does not treat depression. This is evidenced by the following case history. A 46 year old man presented with a 3 year history of depression that began after the death of his mother. His medications included Sertraline (100 mg), selective serotonin reuptake inhibitor (SSRI). He complained of continued depressive symptoms in spite of pharmacologic treatment. He met DSM -IV criteria for major depressive disorder; his BDI-II score was 24. He received 24 units of Botulinum toxin -A into the lateral orbicularis oculi (crows feet) and 8 units of Botulinum toxin -A into the frontalis (mid-forehead) **using the methods described in the specification (in the US).** Six weeks later he remained clinically depressed and his BDI-II score was 25.

Following this treatment, the same man was treated by injection of 29 units of Botulinum toxin-A treatment **into his corrugator supercilii and procerus muscles using the methods described and claimed in the present application (see claims 1, 4-7, 8, 12-15 and 23).** Six weeks later he was no longer clinically depressed and his BDI-II score was 7. Thus, depression was treated by injection of Botulinum toxin into the corrugator and procerus muscles but not into the obicularis oculi or the frontalis muscles. This result was substantially unexpected, and could not be predicted from the teachings of Jahanshahi et al., Binder, Carruthers et al., and/or Wagstaff et al., in any combination.

5. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of the Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.



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Eric Finzi, M.D., Ph.D.

Date